

AMENDMENTS TO THE CLAIMS:

Please incorporate the following amendments into the claims of the subject application.

1-33. **(canceled)**

34. **(previously presented)** The method of claim 69 or 77 wherein the compound is determined to be a compound that reduces the activity of an active receptor state of said constitutively activated GPCR.

35-44. **(canceled)**

45. **(currently amended)** The method of claim 69 or 77 wherein the third intracellular loop of the endogenous **constitutively activated** GPCR comprises the following sequence:

X1BBHyX2

wherein X1 is an amino acid; B is a basic amino acid; Hy is a hydrophobic amino acid; and X2 is an amino acid.

46. **(original)** The method of claim 45 wherein X1 is glycine.

47. **(original)** The method of claim 45 wherein X1 is lysine.

48. **(original)** The method of claim 45 wherein Hy is alanine.

49. **(original)** The method of claim 45 wherein X2 is lysine.

50. **(original)** The method of claim 45 wherein X2 is arginine.

51. **(original)** The method of claim 45 wherein X2 is glutamic acid.

52. (currently amended) The method of claim 69 or 77 wherein the second intracellular loop of the endogenous constitutively activated GPCR comprises the following sequence:

XRY

wherein X can be any amino acid other than aspartic acid; R is arginine; and Y is tyrosine.

53-60. (canceled)

61. (original) The method of claim 45 wherein the sequence XIBBH_yX₂ is an endogenous sequence.

62. (original) The method of claim 52 wherein the sequence XRY is an endogenous sequence.

63-68. (canceled)

69. (currently amended) A method for directly identifying a non-endogenous candidate compound as a compound that stimulates an endogenous G protein coupled receptor (GPCR) or reduces the activity of an active receptor state of an endogenous GPCR, wherein an endogenous ligand for said endogenous GPCR has not been identified ~~and wherein said endogenous GPCR comprises a mutation in its amino acid sequence so as to render it constitutively active~~, said method comprising the steps of:

(a) obtaining a constitutively activated form of said endogenous GPCR, wherein said constitutively activated GPCR comprises a mutation in its amino acid sequence that increases its constitutive activity relative to said endogenous GPCR;

(b) contacting the non-endogenous candidate compound with said constitutively activated GPCR;

(b) determining (c) analyzing whether said non-endogenous candidate compound is a compound that stimulates said endogenous GPCR or reduces the activity of an active receptor state of said endogenous GPCR, by measuring the ability of the candidate compound to stimulate or inhibit functionality of said constitutively activated GPCR, respectively.

70-76. (canceled)

77. (currently amended) A method for directly identifying a non-endogenous compound with compound efficacy as to an endogenous orphan GPCR, the method comprising the steps of:

(a) ~~subjecting said endogenous orphan GPCR to constitutive receptor activation to create a constitutively activated orphan GPCR obtaining a constitutively activated form of said endogenous orphan GPCR, wherein said constitutively activated GPCR comprises a mutation in its amino acid sequence that increases its constitutive activity relative to the endogenous orphan GPCR;~~

(b) contacting the constitutively activated **orphan** GPCR with the non-endogenous compound;

(c) ~~comparing analyzing~~ the functionality of the constitutively activated **orphan** GPCR in the presence and absence of the non-endogenous compound; and

(d) identifying the non-endogenous compound as having compound efficacy if the presence of the compound measurably alters the functionality of the **endogenous** constitutively activated **orphan** GPCR as compared to the functionality of the **endogenous** constitutively activated **orphan** GPCR in the absence of the compound.

78. (canceled)

79. (currently amended) The method of claim 77, wherein said functionality of the constitutively activated **orphan** GPCR is binding to GTP.

80. (canceled)

Please add the following claim:

81. (New) The method of claim 69 or 77, wherein said method is performed in a laboratory or research setting.